REF 800900 NeuMoDx™ HSV 1/2 Calibrators

Rx Only

CAUTION: For US Export Only

IVD For *In Vitro* Diagnostic Use with the NeuMoDx™ HSV 1/2 Quant Test Strip on the NeuMoDx™ 288 and NeuMoDx™ 96 Molecular Systems

*This package insert must be read carefully prior to product use. Package insert instructions must be followed accordingly.*
*Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.*
*For detailed instructions, refer to the NeuMoDx™ 288 Molecular System Operator's Manual; P/N 40600108*
*For detailed instructions, refer to the NeuMoDx™ 96 Molecular System Operator's Manual; P/N 40600317*
*See also the NeuMoDx™ HSV 1/2 Quant Test Strip Instructions For Use (package insert)*

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## INTENDED USE

The NeuMoDx™ HSV 1/2 Calibrators are intended for use with the NeuMoDx™ HSV 1/2 Quant Assay to establish a calibration coefficient associated with a particular lot of the NeuMoDx™ HSV 1/2 Quant Test Strip and used in conjunction with a standard curve to perform an accurate quantitative in vitro diagnostic test on the NeuMoDx™ 288 Molecular System or NeuMoDx™ 96 Molecular System (NeuMoDx™ System(s)) to quantify and differentiate of Herpes simplex virus type 1 (HSV-1, Human alphaherpesvirus 1) DNA and/or Herpes simplex virus type 2 (HSV-2, Human alphaherpesvirus 2) DNA.

## SUMMARY AND EXPLANATION

The NeuMoDx™ HSV 1/2 Calibrators are provided in a kit which contains 3 sets of calibrators for HSV-1, 3 sets of calibrators for HSV-2, two vials of NeuMoDx™ HSV 1/2 Calibrators Buffer, and 12 empty tubes.

Each of the HSV-1 calibrator sets is composed of one low positive and one high positive calibrator sealed in a single aluminum pouch with a small orange desiccant sachet, and each of the HSV-2 Calibrator sets for HSV-2 is composed of one low positive and one high positive calibrator sealed in a single aluminum pouch with a small orange desiccant sachet.

A set of one Low positive and one High Positive Calibrator for each target are processed every 90 days, or with every new lot of NeuMoDx™ HSV 1/2 Quant Test Strips to establish a valid calibration of the NeuMoDx™ HSV 1/2 Quant Assay. HSV-1 and HSV-2 calibrators contain a dried pellet of synthetic HSV-1 and HSV-2 target nucleic acid at 5.12 $\log_{10}$ copies/mL or 3.12 $\log_{10}$ copies/mL for the High and Low Calibrator, respectively. The dried HSV-1/HSV-2 Calibrators must be hydrated using the NeuMoDx™ HSV 1/2 Calibrators Buffer present in the kit.
The NeuMoDx™ HSV 1/2 Quant Assay combines automated DNA extraction, amplification, and detection by real-time PCR to enable the quantitative detection of HSV-1 and/or HSV-2 DNA in human plasma.

The NeuMoDx™ HSV 1/2 Calibrators will be applied to the stored standard curve and used to generate a calibration coefficient, which is used to automatically adjust the standard curve for slight variations across systems or test strip lots. Accurate quantitation of the HSV-1 DNA and HSV-2 DNA in the human clinical samples being tested can then be provided utilizing both the standard curve and the system/lot specific calibration coefficient.

## PRINCIPLES OF THE PROCEDURE

The NeuMoDx™ HSV 1/2 Calibrators are necessary for the calibration of the whole testing workflow. One set of these calibrators – consisting of 1 high calibrator and 1 low calibrator for each target– is to be processed, every 90 days or with the change of a system, software or test strip reagent lot; the system will automatically process each calibrator in triplicate. Such routine processing of the NeuMoDx™ HSV 1/2 Calibrators enables the laboratories to ensure efficacy of the test results for human clinical specimens processed within the validity period.

Software on the NeuMoDx™ System automatically alerts the operator when a calibration is required. During processing, criteria for acceptance of the calibrator are automatically verified by the NeuMoDx™ System software. If less than two of the calibrator replicates are valid, the software automatically invalidates the run. Samples in an invalidated run must be retested using a new set of calibrators and controls.

Upon successful processing of the NeuMoDx™ HSV 1/2 Calibrators, the system software automatically records the validity of the processed calibrators for a period of 90 days unless there is a change to the system that causes the validity period to expire. The NeuMoDx™ System software will automatically notify the user to process these calibrators when the previously processed calibrator validity period has expired.

## REAGENTS / CONSUMABLES

### *Material Provided*

| REF | Contents | Set per unit | Total tests per set |
|---|---|---|---|
| 800900 | NeuMoDx™ HSV 1/2 Calibrators<br>*Single use sets of HSV-1 High and Low Calibrators and HSV-2 High and Low Calibrators to establish standard curves*<br>*(1 vial of 5.12 $log_{10}$ copies/mL dried DNA and 1 vial of 3.12 $log_{10}$ copies/mL dried DNA = 1 set)* | 1 set | 3 |

### *Reagents and Consumables Required but Not Provided (Available Separately from NeuMoDx)*

| REF | Contents |
|---|---|
| 202400 | NeuMoDx™ HSV 1/2 Quant Test Strip<br>*Freeze-Dried PCR reagents containing HSV-1 specific TaqMan® probes and primers, HSV-2 specific TaqMan® probes and primers in addition to SPC1-specific TaqMan® probe and primers.* |
| 100200 | NeuMoDx™ Extraction Plate<br>*Dried paramagnetic particles, Lytic enzyme, and sample process controls.* |
| 900901 | NeuMoDx™ HSV 1/2 External Controls<br>*Single use sets of HSV-1 and HSV-2 Positive and Negative Controls to establish daily validity of NeuMoDx™ Quant Assay.* |
| 400400 | NeuMoDx™ Lysis Buffer 1 |
| 400100 | NeuMoDx™ Wash Reagent |
| 400200 | NeuMoDx™ Release Reagent |
| 100100 | NeuMoDx™ Cartridge |
| 235903 | Hamilton CO-RE Tips (300 µL) with Filters |
| 235905 | Hamilton CO-RE Tips (1000 µL) with Filters |

For the reagents and consumables details please refers to the related insert

### *Instrumentation Required*

NeuMoDx™ 288 Molecular System (REF 500100) or NeuMoDx™ 96 Molecular System (REF 500200).

## WARNINGS & PRECAUTIONS

- The NeuMoDx™ HSV 1/2 Calibrators are for *in vitro* diagnostic use only with the NeuMoDx™ HSV 1/2 Quant Test Strip as implemented on the NeuMoDx™ Systems.
- Do not use the NeuMoDx™ HSV 1/2 Calibrators after the listed expiration date.
- Do not use the NeuMoDx™ HSV 1/2 Calibrators if the safety seal is broken or if the packaging is damaged upon arrival.
- Do not use consumables or reagents if the protective pouch is open or broken upon arrival.
- Do not mix up reagents for amplification from other commercial kits.
- Do not reuse.
- Keep the NeuMoDx™ HSV 1/2 Calibrators protected from humidity in their aluminium envelopes with dedicated small orange desiccant sachet.
- Because the calibrators contain HSV-1 and HSV-2 target material, they should be handled carefully as cross-contamination with test samples could produce a false-positive result.
- Always handle specimens as if they are infectious and in accordance with safe laboratory procedures such as those described in accordance with the OSHA Standard on Bloodborne Pathogens[1], Biosafety Level 2[2] or other appropriate biosafety practices[3,4] should be used for materials that contain or are suspected of containing infectious agents.
- Do not pipette by mouth. Do not smoke, drink, or eat in areas where specimens or reagents are being handled.
- Dispose of unused reagents and waste in accordance with country, federal, provincial, state and local regulations.
- Clean, powder-free, nitrile gloves should be worn when handling all NeuMoDx™ reagents and consumables.
- Safety Data Sheets (SDS) are provided for each reagent (as applicable) at www.neumodx.com/client-resources.
- A vertical bar in the text margin indicates changes in comparison to the previous IFU version.
- Wash hands thoroughly after performing the test.

## PRODUCT STORAGE, HANDLING & STABILITY

- The NeuMoDx™ HSV 1/2 Calibrators are shipped at Room Temperature (+15 °C/+30 °C).
- It is recommended that the NeuMoDx™ HSV 1/2 Calibrators be stored at +15 °C/+30 °C to ensure stability.
- Calibrator vials (reconstituted calibrators and/or empty tubes) are intended for single use only. After use, discard the reconstituted NeuMoDx™ HSV 1/2 Calibrators.
- Discard any unused material after use in biohazard waste as the material contains non-infectious target DNA and could cause a contamination risk.

## INSTRUCTIONS FOR USE

1. NeuMoDx™ HSV 1/2 Calibrators (REF 800900) must be processed under the following scenarios:
    a. Validity of previously established calibration has expired (past 90 days).
    b. Calibration validity has not been established on the NeuMoDx™ System(s).
    c. Calibration validity has not been established with a new lot of NeuMoDx™ HSV 1/2 Quant Test Strips.
    d. The NeuMoDx™ System software or ADF has been modified.
2. The NeuMoDx™ HSV 1/2 Quant Assay uses with two different calibration curves which are embedded in the HSV 1/2 Assay Definition File (ADF), one for HSV-1 and one for HSV-2.
3. If a valid calibration does not exist, the NeuMoDx™ System will prompt the user to process calibrators (and external controls) before samples are processed.
4. If calibrators are required, reconstitute the NeuMoDx™ HSV 1/2 Calibrators (1 set for HSV-1 - 1 high calibrator and 1 low calibrator per reagent lot, 1 set for HSV-2 - 1 high calibrator and 1 low calibrator per reagent lot) following the steps below:

| NeuMoDx™ HSV 1/2 Calibrators | Label Color Scheme | Barcode IDs |
|---|---|---|
| HSV-1 | | |
| High Calibrator (HC) | Green | HCHV1 |
| Low Calibrator (LC) | Blue | LCHV1 |
| HSV-2 | | |
| High Calibrator (HC) | Orange | HCHV2 |
| Low Calibrator (LC) | Purple | LCHV2 |

5. Cut the aluminum pouches of the required calibrator/s at the point indicated by the lateral notches.
6. Remove NeuMoDx™ HSV-1 Calibrator tubes (HIGH and LOW) and/or NeuMoDx™ HSV-2 Calibrator tubes (HIGH and LOW) from the pouches immediately before use.
7. Ensure that before using the pouches, they are well-sealed with desiccant sachets still inside. Use only undamaged packages.
8. Discard the aluminum pouches and their contents if the desiccant sachets turn from orange to green.
9. Centrifuge the NeuMoDx™ HSV-1 Calibrator tubes (HIGH and LOW) and/or NeuMoDx™ HSV-2 Calibrator tubes (HIGH and LOW) prior to opening them to ensure that DNA is at the bottom of the tube.
10. Vortex the NeuMoDx™ HSV 1/2 Calibrators Buffer and reconstitute each NeuMoDx™ HSV-1 Calibrator tube (HIGH and LOW) and/or NeuMoDx™ HSV-2 Calibrator tube with 1900 µL of NeuMoDx™ HSV 1/2 Calibrators Buffer. The reconstituted calibrator tubes are intended for single use only.
11. Cap each Calibrator tube and vortex it for 30 seconds until the dried DNA is resuspended.
12. Centrifuge the NeuMoDx™ HSV-1 Calibrator tubes (HIGH and LOW) and/or NeuMoDx™ HSV-2 Calibrator tubes (HIGH and LOW) for few seconds at medium speed to remove any residue from the cap and eliminate bubbles/foam.
13. Incubate for at least 20 minutes at room temperature before use.
14. Vortex the NeuMoDx™ HSV-1 Calibrator tubes (HIGH and LOW) and/or NeuMoDxTM HSV-2 Calibrator tubes (HIGH and LOW) for a few seconds at medium speed and centrifuge them for a few seconds at medium speed.
15. Transfer all the contents of each tube into a secondary empty labelled tube (NeuMoDx™ HSV-1 High Calibrator (HC) tube, NeuMoDx™ HSV-1 Low Calibrator (LC) tube, NeuMoDx™ HSV-2 High Calibrator (HC) tube, NeuMoDx™ HSV-2 Low Calibrator (LC) tube included in the kit). Both reconstituted calibrators and secondary tubes are intended for single use only.
16. Load the calibrator tubes into a standard 32-Tube Specimen Carrier.
17. Place the Specimen Tube Carrier on the Autoloader shelf and use the touchscreen to load the carrier into the NeuMoDx™ System.

18. The NeuMoDx™ System will recognize the barcode and start processing the specimen tubes unless reagents or consumables required for testing are not available.
19. To generate valid results, at least 2 out of the 3 replicates must yield results within predefined parameters. The low calibrator nominal target is 3.12 $log_{10}$ copies/mL and the high calibrator nominal target is 5.12 $log_{10}$ copies/mL.

| NeuMoDx™ HSV 1/2 Calibrators | Result |
|---|---|
| HSV-1 | |
| High Calibrator (HC) | At least 2/3 calibrators Valid |
| Low Calibrator (LC) | At least 2/3 calibrators Valid |
| HSV-2 | |
| High Calibrator (HC) | At least 2/3 calibrators Valid |
| Low Calibrator (LC) | At least 2/3 calibrators Valid |

20. Discrepant result handling for calibrators should be performed as follows:
    a. If one or both the calibrators fail the validity check for HSV-1 or HSV-2, repeat processing of the failed calibrator(s) using a new vial. In the event only one calibrator fails validity, it is possible to only repeat the failed calibrator as system does not require the user to reprocess both calibrators.
    b. If problem persists, contact QIAGEN technical support.
21. NeuMoDx™ HSV 1/2 External Controls (REF 900901) must be processed after calibrator validity has been established, prior to obtaining test results from human clinical samples.

## LIMITATIONS

1. The NeuMoDx™ HSV 1/2 Calibrators can only be used in conjunction with the NeuMoDx™ HSV 1/2 Quant Test Strips on the NeuMoDx™ Molecular Systems.
2. A valid calibration of the NeuMoDx™ HSV 1/2 Quant Test Strip using NeuMoDx™ HSV 1/2 Calibrators (REF 800900) is required before the NeuMoDx™ HSV 1/2 External Controls (REF 900901) can be processed.
3. Erroneous results could occur from improper handling, storage, or other technical error.
4. Operation of the NeuMoDx™ Molecular System is limited to use by personnel trained on the use of the NeuMoDx™ Molecular System.

## REFERENCES

1. US Department of Labor, Occupational Safety and Health Administration. 29 CFR Part 1910.1030. Bloodborne Pathogens, https://www.osha.gov/lawsregs/regulations/standardnumber/1910/1910.1030
2. US Department of Health and Human Services. Biosafety in Microbiological and Biomedical Laboratories, 5th Ed. Washington,DC: US Government Printing Office, January 2009.
3. World Health Organization. Laboratory Biosafety Manual, 3rd ed. Geneva: World Health Organization, 2004.
4. CLSI. Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline — Fourth Edition (M29-A4). Clinical and Laboratory Standards Institute, 2014.

## TRADEMARKS

## SYMBOLS

| SYMBOL | MEANING |
|---|---|
| Rx Only | Prescription use only |
|  | Manufacturer |
|  | Distributor |
| IVD | *In vitro* diagnostic medical device |
| REF | Catalog number |
| LOT | Batch code |
|  | Consult instruction for use |
|  | Caution, consult accompanying documents |
|  | Temperature limitation |
|  | Keep dry |
|  | Do not re-use |
|  | Do not expose to the light |
|  | Contains sufficient for <*n*> tests |
|  | Use by |


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